

Women and Ischemia Syndrome Evaluation (WISE) Diagnosis and Pathophysiology of Ischemic Heart Disease Workshop

October 2-4, 2002

Session 3

1. Topic and Author

Pathology of Acute Ischemic Syndrome.

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2. Where we stand in 2002. Overview/rationale for inclusion of topic.

Coronary atherosclerosis is a complex disease. Few morphologic studies have addressed differences between men and women in acute coronary syndromes. There are two distinct patterns of the plaque in which thrombosis occurs: plaque ruptures (underlying 50-60% of coronary thrombi), and plaque erosions (underlying 35-50% of acute thrombi) in patients dying a sudden coronary death. Features of plaque erosion that contrast with plaque rupture are a predilection for women and younger patients, and a lesser degree of underlying luminal narrowing. In women < 50 years the main cause of thrombosis is plaque erosion, and the only known risk factor predictive of erosion is smoking. Plaque ruptures are the main cause of thrombosis in women older than 50 years and there is, like men an association with high total cholesterol. In men, low high density lipoprotein cholesterol, and high ratios are predictive of rupture, but not in women. Acute thrombosis is associated with smoking; hypertensives have a significantly lower incidence of coronary thrombosis, but when it occurs, the cause is more frequently rupture than erosion. There is no association of glucose intolerance with plaque morphology. Thus, risk factors modify underlying plaque morphology and are predictors of the mechanism of sudden cardiac death. Similarly, in acute myocardial infarction, plaque rupture is the main cause of thrombosis; plaque erosion is less frequent but is significantly more common in women than men. Plaque burden index is higher in men than women with acute coronary syndromes such as sudden death. Patients with plaque erosion have less diffuse disease than plaque rupture. Women for each decade have less coronary calcification until the seventh decade when it begins to equalize with men. The only predictor of calcification in women is the presence of diabetes mellitus.

3. Current challenges and the most important issues for future research

Why do women have erosions at < 50 years?

Is vasospasm an important factor in women with erosion?

Is there less diffuse coronary disease in women with erosion?

Is inflammation an important mechanism of erosion?

What inflammatory markers may be predictive of CAD in women?

Is embolic disease more frequent in women than men?

Is there poor collateralization of coronary arteries in women leading to higher mortality from coronary disease?

4. Current challenges in the areas of communicating messages to health care community, patients and the public

There is poor public awareness that coronary disease death rates are high in women.

Education of emergency rooms and family physicians of the type of risk factors for coronary heart disease in women.

Erosion is not easily detected by coronary angiography, and there is need for better diagnostic tools.

5. Translating new findings to improved diagnosis and treatment/saving lives.

Need better modalities for the detection of both silent and overt coronary heart disease in women.

Diabetic patients have more diffuse disease and angiography is a poor tool to detect it.

Women do not tend to seek medical help for symptoms of chest pain and may be related to physician attitude.

Understanding of vulnerable plaque and determine if detected will it lead to symptomatic heart disease or increase in plaque burden.

6. References

1. Virmani R, Kolodgie FD, Burke AP, Farb A, Schwartz SM. Lessons from sudden coronary death: a comprehensive morphological classification scheme for atherosclerotic lesions. *Arterioscler Thromb Vasc Biol.* 2000;20:1262-75.
2. Farb A, Burke AP, Tang AL, Liang TY, Mannan P, Smialek J, Virmani R. Coronary plaque erosion without rupture into a lipid core. A frequent cause of coronary thrombosis in sudden coronary death. *Circulation.* 1996;93:1354-63.
3. Burke AP, Farb A, Malcom GT, Liang Y, Smialek J, Virmani R. Effect of risk factors on the mechanism of acute thrombosis and sudden coronary death in women. *Circulation.* 1998;97:2110-6.
4. Burke AP, Farb A, Malcom G, Virmani R. Effect of menopause on plaque morphologic characteristics in coronary atherosclerosis. *Am Heart J.* 2001;141:S58-62.
5. Burke AP, Farb A, Liang YH, Smialek J, Virmani R. Effect of hypertension and cardiac hypertrophy on coronary artery morphology in sudden cardiac death. *Circulation.* 1996;94:3138-45.
6. Burke AP, Weber DK, Kolodgie FD, Farb A, Taylor AJ, Virmani R. Pathophysiology of calcium deposition in coronary arteries. *Herz.* 2001;26:239-44.
7. Burke AP, Kolodgie FD, Farb A, Weber DK, Malcom GT, Smialek J, Virmani R. Healed plaque ruptures and sudden coronary death: evidence that subclinical rupture has a role in plaque progression. *Circulation.* 2001;103:934-40.
8. Burke AP, Tracy RP, Kolodgie F, Malcom GT, Zieske A, Kutys R, Pestaner J, Smialek J, Virmani R. Elevated C-reactive protein values and atherosclerosis in sudden coronary death: association with different pathologies. *Circulation.* 2002;105:2019-23.
9. Burke AP, Kolodgie FD, Farb A, Weber D, Virmani R. Morphological predictors of arterial remodeling in coronary atherosclerosis. *Circulation.* 2002;105:297-303.